Inaccuracies in “Long-term health outcomes of children born to mothers with hyperemesis gravidarum: a systematic review and meta-analysis”

Marlena S Fejzo, PhD
Department of Maternal Fetal Medicine, Keck School of Medicine, University of Southern California, Los Angeles, California, USA.
MSF is a paid consultant for Materna Biosciences, Inc.

Kimber W MacGibbon RN, Executive Director
Hyperemesis Education and Research Foundation, Clackamas, Oregon, USA.
No conflicts of interest to declare.

Patrick M Mullin MD MPH
Department of Maternal Fetal Medicine, Keck School of Medicine, University of Southern California, Los Angeles, California, USA.
No conflicts of interest to declare.

Corresponding Author
Marlena S Fejzo, PhD
Department of Maternal Fetal Medicine, Keck School of Medicine, University of Southern California, Los Angeles, California, USA.
MSF is a paid consultant for Materna Biosciences, Inc.
fejzo@usc.edu
Dear Editor,

Association of Hyperemesis Gravidarum (HG) with neurodevelopmental outcomes and smaller brains may motivate providers to take HG more seriously. This is critical because of the adverse offspring outcomes and because 25.5% of HG cases report suicidal ideation, associated with perception of care.¹

Therefore, it is concerning that a meta-analysis of long-term outcomes associated with HG misrepresented our studies based on their scale.²

A score of 0 was assigned for:

1. **“Representativeness”** because “Participants self-enrolled through the HER foundation, which may lead to selection bias, since patients with more severe HG/prolonged disease course may have been more likely to apply.” (Nijsten, personal communication) Participants were enrolled from all over the US, potentially more representative than one setting - i.e. some hospitals service primarily low-income uninsured ethnic minorities- in one study, scored representative, only 16% of children were white-unrepresentative of the US population.

   Nijsten has no evidence patients with more severe/prolonged HG were more likely to enroll, but does cite “ICD codes (are) only valid for diagnosing women with mild HG, (and were used) in the 4 largest studies included,” thereby including studies of mild disease while excluding studies they believe are more inclusive of severe disease.

2. **“Ascertainment of exposure”** because “HG definition was based on self-reports first (and then verified by medical records). This could have resulted in recall bias.” Participant’s recall was fact-checked with medical records. IV fluid treatment for HG was our clinical criteria because it is hard to forget. This choice is validated as we identified a nausea/vomiting hormone gene associated with HG using overlapping participants.³

3. **“Outcome of interest not present at start”** because “Participants were not prospectively recruited from a predefined population, but recruited retrospectively from people that visited the HER website.” This is incorrect and their own follow-up study, designed the same way, was defined as “a prospective cohort study.” ⁴

4. **“Comparability”** because “match(ing) controls and cases based on offspring’ age and sex was not the case in your studies.” Our cases and controls were shown in the manuscript to NOT be significantly different for child’s age in our 2015 and 2019 studies. Sex biases toward the null. In our 2015 paper both age and gender of offspring of cases and controls was not significantly different.

   Inaccurate ratings assigned to our studies contributes to bias and may underestimate neurodevelopmental findings. The study should be repeated to address concerning errors/biases before drawing conclusions.
REFERENCES


